Remarks

Claims 41-52 are pending in this application. No claim amendments are made in this paper, and thus, no new matter has been introduced.

Applicant respectfully submits that all of the pending claims are allowable for at least the following reasons.

A. The Rejection Under 35 U.S.C. § 103 Should Be Withdrawn

On pages 2-12 of the Office Action, claims 41-52 are rejected over Scott *et al.*, *Br. J. Pharmacol.*, 111: 97-102 (1994) ("Scott"), in view of WO 94/00114 by Young *et al.* ("Young") and an excerpt from *Harrison's Principles of Internal Medicine*, 13th Ed., pp. 162-168 (1994) ("Harrison"), and in further view of Gundlah *et al.*, *Pharmacology and Experimental Therapeutics*, 283(2): 581-591 (1997) ("Gundlah"). Applicant respectfully traverses this rejection.

At the outset, Applicant respectfully reiterates that the claims are not obvious for at least the reasons set forth in his previous response of June 26, 2007, which is incorporated herein by reference. Specifically, Applicant respectfully points out that: 1) the combination of references cited by the Examiner does not teach or suggest enantiomerically pure (S)-didesmethylsibutramine; 2) even assuming, *arguendo*, the references somehow suggests enantiomerically pure (S)-didesmethylsibutramine, they clearly do not teach or suggest the use of enantiomerically pure (S)-didesmethylsibutramine for the treatment of narcolepsy; and 3) Luscombe's teaching that didesmethylsibutramine and sibutramine have similar *in vivo* activities would not have prompted those skilled in the art to investigate didesmethylsibutramine, much less enantiomerically pure (S)-didesmethylsibutramine. (*See* Applicant's response of June 26, 2007, pages 2-4).

In response, the Examiner offers the following: 1) "Applicant's conclusory statement that there is no specific suggestion or teaching in the references to combine prior art" is "foreclosed" by the decision in *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007) (Office Action, page 4); 2) Luscombe's teaching that sibutramine and didesmethylsibutramine exhibit similar *in vivo* activities "would reasonably have provided motivation ... to investigate the therapeutic effects of enantiomerically pure (S)-didesmethylsibutramine" (*Id.*, pages 4-5); and 3) "Applicant's assertion that the cited references do not teach enantiomerically pure (S)-didesmethylsibutramine ignores the fact that independent claim 1 encompasses varying degrees of enantiomeric purity," and that "in the absence of a clear specific definition," the term is construed to encompass racemic mixtures. (*Id.*). Applicant respectfully disagrees for at least the following reasons.

First, with regard to the Examiner's allegation that the requirement of specific teaching, suggestion, or motivation ("TSM test") is "foreclosed" by the *KSR* decision, Applicant respectfully points out that the Examiner's position is legally incorrect. In fact, the *KSR* decision indicated that while the TSM test is not the sole method for determining obviousness, it may still be a factor. (*KSR*, 127 S.Ct. at 1741 ("[w]hen it first established [the TSM test], the Court...captured a helpful insight.")).

In addition, Applicant respectfully points out that no assertion that "specific" motivation is required in establishing a *prima facie* case was made in his previous response. Rather, it was pointed out that the combination of Scott (which discloses that didesmethylsibutramine has activity similar to sibutramine *in vivo*) and Young (which discloses isomers of sibutramine) would not have prompted those skilled in the art to even investigate didesmethylsibutramine, much less (S)-didesmethylsibutramine. This is because Scott, like Luscombe reference provided by Applicant, discloses that *in vivo* activities of sibutramine and didesmethylsibutramine are similar. Therefore, those skilled in the art, even if they were looking for an alternative to sibutramine, would not have been led to investigate didesmethylsibutramine in the face of Scott's and Luscombe's disclosure that *in vivo* activity[1] of didesmethylsibutramine has little difference from that of sibutramine.

In other words, those skilled in the art would have had no reason to spend the effort and resources in investigating didesmethylsibutramine, much less (S)-didesmethylsibutramine, as an alternative to sibutramine (a known, well-established compound), unless there was a reasonable basis to believe that didesmethylsibutramine would be significantly more advantageous than sibutramine. As was pointed out above, Scott and Luscombe provide contrary result – that *in vivo* activity of didesmethylsibutramine is not significantly better than that of sibutramine[2]. Therefore, Applicant respectfully submits that those skilled in the art would not have had any motivation to investigate didesmethylsibutramine at the first instance.

Moreover, even assuming, *arguendo*, that those skilled in the art were somehow led to investigate (S)-didesmethylsibutramine, its use for the treatment of narcolepsy would still have not been obvious. In this regard, Applicant respectfully points out that the blanket statement that certain symptoms of narcolepsy can be treated with "antidepressants" (as disclosed in Harrison, the third reference cited by the Examiner) does

---

[1] It is evident that *in vivo* activity is of critical importance in assessing the therapeutic potential of a compound.

[2] This also addresses the Examiner's second allegation that Luscombe would have actually motivated those skilled in the art.

not provide any basis to conclude that any and all antidepressants are effective in treating such symptoms.

This is evidenced by the disclosure of Harrison itself. In the very portion referred to by the Examiner, Harrison, while indicating that antidepressants may be effective in treating certain symptoms of narcolepsy, and that protriptyline is commonly used, also indicates that "compounds including viloxzine hydrochloride and fluoxetine are under evaluation" for narcolepsy. (Harrison, page 167, last paragraph). This clearly implies that each and every antidepressant must be separately evaluated for their efficacy and/or safety for the treatment of narcolepsy, and that purported efficacy of one antidepressant may not be interpolated to any other antidepressants. Thus, Harrison, at most may have rendered the treatment of narcolepsy using (S)-didesmethylsibutramine "obvious to try." As well-settled, "obvious to try" is not a proper legal standard for obviousness, before or after *KSR*. Consequently, Applicant respectfully submits that the combination of references cited by the Examiner would not have led those skilled in the art to arrive at the claimed method.

Finally, with regard to the Examiner's allegation that the term "enantiomerically pure (S)-didesmethylsibutramine" could be interpreted to encompass the racemic mixture, Applicant respectfully points out that such an interpretation is arbitrary and wholly baseless. This is because, contrary to the Examiner's allegation that "a clear specific definition" is lacking for the term in the specification, Applicant respectfully points out that the term is indeed clearly and specifically defined in the specification.

In this regard, Applicant respectfully invites the Examiner's attention to page 5 of the specification. There, it is clearly stated that the term "enantiomerically pure" means one enantiomer of a compound that is "substantially free" of the opposite enantiomer of the compound. (Specification, page 5, lines 16-19). In turn, the specification clearly defines that being "substantially free" of a compound means that the compound is present in less than about 20%, 10%, 5%, or 3% of the weight of the composition. Consequently, based on this clear, specific definition, Applicant respectfully points out that "enantiomerically pure (S)-didesmethylsibutramine" cannot encompass racemic didesmethylsibutramine, and thus, the Examiner's third allegation is without merit[3].

[3] Be that as it may, if the Examiner believes that amending claim 1 to specify the term "enantiomerically pure (S)-didesmethylsibutramine" in terms of the weight percentage would expedite the prosecution of this application, Applicant would be amenable to such an amendment.

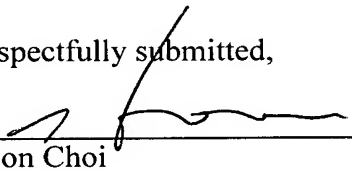
Conclusion

For at least the foregoing reasons, Applicant submits that all of the pending claims are allowable, and thus, respectfully requests that the rejection of the claims under 35 U.S.C. § 103 be withdrawn.

No fee is believed due for this submission. If any fees are required, however, please charge such fee(s) to Deposit Account No. 503013.

Respectfully submitted,

Date October 31, 2007



L0209

Hoon Choi (Ltd. Recog. No.)
Jones Day

For Anthony M. Insogna (Reg. No. 35,203)
Jones Day
12265 El Camino Real, Suite 200
San Diego, CA 92130
(858) 314-1200